660.51
S993
660

Organic Chemical Bulletin

DPi

Volume 24 • 1952 • Number 3

Address inquiries to
Eastman Organic Chemicals Dept.
Distillation Products Industries
Division of Eastman Kodak Company
Rochester 3, N. Y.

PUBLISHED BY THE RESEARCH LABORATORIES OF THE EASTMAN KODAK COMPANY

Recent Advances in Brominations by N-Bromosuccinimide and Related Compounds*

By JOHN D. CAWLEY

The bromination of olefins in the "allyl

position," i.e., the transformation by N-bromoamides, and especially by N-bromosuccinimide (NBS), has been widely used by organic chemists since the demonstration of its generality by Ziegler et al. in 1942 (1). The discovery of the catalytic effect of peroxides (2), which made possible the bromination of carbonyl compounds and alkyl chains attached to aryl groups, broadened still further the scope of the reaction. The literature has been thoroughly reviewed to June 1, 1948 (3). Some of the more important work which has appeared between this date and January 1, 1951, will be discussed here.

A few apparent generalities concerning the action of NBS were announced. From a study of the bromination of variously methylated naphthalenes, coumarins, pyrones, thiophenes, and furans, Lecocq (4) concluded that the ease of bromination increased and the stability of the brominated products decreased as the aromaticity of the rings decreased. The compounds, 2,3-, 2,6-, and 2,7-dimethylnaphthalene, could each be selectively brominated at the 3-, 6-, and 7-methyl groups to give 2-methyl-3-, 6-, and 7-bromomethylnaphthalene, the 2-methyl group in each case remaining unattacked.

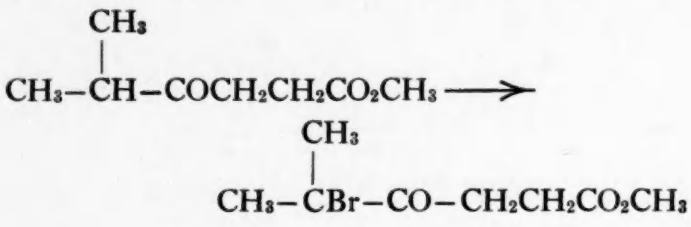
The effect of the ratios of reagents and of the presence or absence of peroxide catalysts on the course of the bromination of 2- and 3-methylthiophene was systematically investigated by Dittmer et al. (5). With equimolar amounts of reactants in the absence of peroxides, bromination by NBS proceeded largely at the nuclear 5- and 2- positions, respectively, but, with peroxide present, almost exclusively at the methyl groups. With excess NBS, simultaneous nuclear-chain bromination took place, and the peroxide was without effect.

In contrast to these generalities, several abnormalities were noted. Braude and Waight (6) found that the presence of amine or quaternary ammonium salts caused cyclohexene and allylbenzene to react with NBS by addition of bromine to the double bond, rather than by the normal substitution of bromine adjacent to the bond. The reaction was not catalyzed by peroxide, showing it did not proceed by a free-radical mechanism, in contrast to the substitution reaction. Aromatic nitrogen heterocycles were found to react anomalously with NBS (7). The methyl group of 2-picoline was

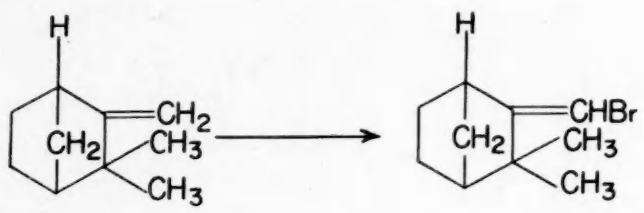
*Communication No. 188, Research Laboratories, Distillation Products Industries, Rochester 3, New York.

not attacked, in contrast to methyl groups attached to aromatic carbocycles. (Buu-Hoi (8), however, has reported success with this reaction.) 9-Methylcarbazole and its 1,2,3,4-tetrahydro derivative gave only nuclearly brominated products.

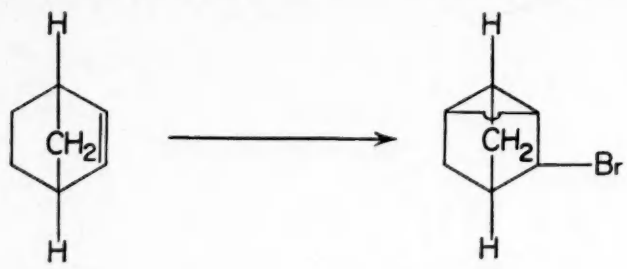
Schindler (9) reported methyl δ,δ-dimethyllevulinate to be brominated at the methine hydrogen at the δ-position, rather than, as is customary (cf. (3), p. 285), at a methylene hydrogen at the β-position.



In contrast to this predilection of methine hydrogen to react, Roberts and Trumbull (10) found that the methine hydrogen attached to the bridgehead of camphene did not react at all, and instead bromination occurred in the vinyl position.



Norbornylene, in which the only allyl hydrogens are also located at the bridgehead, was also brominated at the vinyl position, but here cyclization to 3-bromonortricyclene also occurred (11).



An additional example of bromination in the vinyl position was also encountered by Southwick et al. (12) during a study of the reaction of NBS with various β-phenyl-α,β-unsaturated ketones.

$C_6H_5CH=CHCOCH_3 \longrightarrow$
46% $C_6H_5CHBrCHBrCOCH_3$

$C_6H_5CH=CHCOC_6H_5 \longrightarrow$
57% $C_6H_5CHBrCHBrCOC_6H_5$

$(C_6H_5)_2C=CHCOC_6H_5 \longrightarrow$
68% $(C_6H_5)_2C=CBrCOC_6H_5$

$C_6H_5CH=C(C_6H_5)COC_6H_5 \longrightarrow$
62% geometrical isomer

$(C_6H_5)_2C=C(C_6H_5)COC_6H_5 \longrightarrow$ no reaction

$C_6H_5CH=CBrCOC_6H_5 \longrightarrow$ no reaction

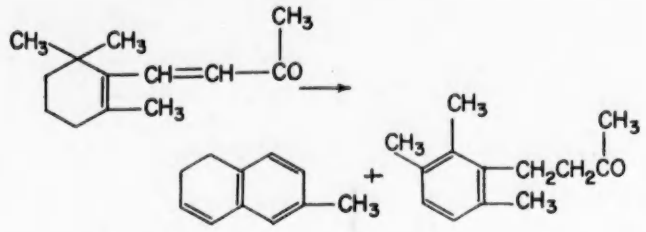
$C_6H_5CH=CHCOCH_2C_6H_5 \longrightarrow$
90-95% $C_6H_5CH=CHCOCHBrC_6H_5$

No consistent explanation for these divergent results could be given.

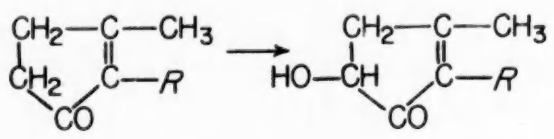
A solvent, usually carbon tetrachloride, is frequently used in reactions with NBS, in order only to ameliorate the otherwise often vigorous reactions, but Bruylants (13) found that the course of the reaction with both *cis*- and *trans*-crotononitrile was profoundly affected by the presence or absence of this solvent. The *cis*-isomer, in the presence of carbon tetrachloride, yielded 8% of a mixture of *cis*- and *trans*-γ-bromocrotononitrile, while in the absence of the solvent there was formed 34% of a mixture of *cis*- and *trans*-α-bromocrotononitrile. The results with *trans*-crotononitrile were similar.

Allylic rearrangements during or after the bromination of △′-olefins have been previously observed (cf. (3)), and Bateman et al. (14) have furnished two additional examples; 1-octene yielded chiefly 1-brom-2-octene, and 1,5-hexadiene gave mainly 1-bromo-2,5-hexadiene.

Karrer and Ochsner (15) were unable to repeat Henbest's (16) briefly reported preparation of dehydro-β-ionone by the bromination and dehydrobromination of β-ionone. The only products isolated were the hydrocarbon 3-dehydroionene and 4-(2,3,6-trimethylphenyl) -2-butanone.



N-Bromosuccinimide was used in synthetic work with varying degrees of success. Crombie et al. (17) investigated the possibility of introducing a hydroxyl group at the 5-position of 2-alkyl-3-methyl-2-cyclopenten-1-ones by bromination, metathesis with silver acetate, and saponification.



With an appropriate group R, the resulting cyclopentenolones would comprise one half of the molecule of the important insecticides, pyrethrin (R = $CH_2CH=CHCH=CH_2$) and cinerin (R = $CH_2CH=CHCH_3$). The scheme was successful when R was *n*-amyl (tetrahydropyrethrone) or *n*-butyl (dihydrocinerone), but failed when R was unsaturated. Unfortunately, R must be unsaturated for high insecticidal activity of the final products.

The introduction of conjugated double bonds into fatty acids such as oleic and linoleic, with resultant enhancement of drying properties, by bromination and dehydrobromination, appears feasible, and Teeter (18) and Sutton and Dutta (19) have explored this possibility. The reaction is not clean, and while some production of conjugation was observed spectroscopically, no clearly defined products were isolated.

The use of N-bromo compounds other than NBS has been limited. A kinetic investigation by Bell and Tantram (20) of the bromination of acetone by N-bromophthalimide revealed that the reaction is catalyzed by acid, which probably functions to promote enolization, bromination of the enol then ensuing. It was also shown that an organic hypobromite could not be the brominating agent, as had previously been postulated by Israel et al. (21).

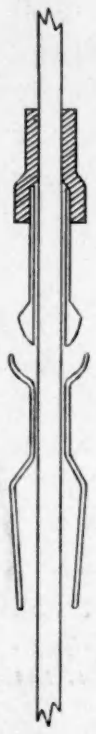
The new reagents, 3-bromo- and 1,3-dibromo-5,5-dimethylhydantoin, introduced by Orazi and Meseri (22), can be prepared in 80% yield from the hydantoin and bromine in the presence of a base and show qualitatively the same reactions as does NBS. They possess the advantages of having somewhat greater stability and solubility and a higher percentage of active bromine.

References

1. Ziegler, K., Spaeth, A., Schaaf, E., Schumann, W., and Winkelmann, E., *Ann.*, **551**, 80 (1942).
2. Schmid, H., and Karrer, P., *Helv. Chim. Acta*, **29**, 573 (1946).
3. Djerassi, C., *Chem. Revs.*, **43**, 271 (1948).
4. Lecocq, J., *Ann. chim.*, **3**, 62 (1948).
5. Dittmer, K., Martin, R., Herz, W., and Cristol, S., *J. Am. Chem. Soc.*, **71**, 1201 (1949).
6. Braude, E., and Waight, E., *Nature*, **164**, 241 (1949).
7. Cosgrove, S., and Waters, W., *J. Chem. Soc.* (*London*), p. 907 (1949).
8. Buu-Hoi, N., *Ann.*, **556**, 1 (1944).
9. Schindler, O., *Pharm. Acta Helv.*, **23**, 273 (1948); *C. A.*, **43**, 3792 (1949).
10. Roberts, J., and Trumbull, Jr., E., *J. Am. Chem. Soc.*, **71**, 1630 (1949).
11. Roberts, J., Trumbull, Jr., E., Bennett, W., and Armstrong, R., *Ibid.*, **72**, 3116 (1950).
12. Southwick, P., Pursglove, L., and Numerof, P., *Ibid.*, **72**, 1600 and 1604 (1950).
13. Bruylants, A., *Bull. soc. chim. belges*, **59**, 107 (1950); *C. A.*, **44**, 7223 (1950).
14. Bateman, L., Cunneen, J., and Koch, H., *Nature*, **164**, 242 (1949).
15. Karrer, P., and Ochsner, P., *Helv. Chim. Acta*, **31**, 2093 (1948).
16. Henbest, H. B., *Nature*, **161**, 481 (1948).
17. Crombie, L., Elliott, M., and Harper, S., *J. Chem. Soc.* (*London*), p. 971 (1950).
18. Teeter, H., *J. Am. Oil Chemists' Soc.*, **25**, 243 (1948).
19. Sutton, D., and Dutta, J., *J. Chem. Soc.* (*London*), p. 939 (1949).
20. Bell, R., and Tantram, A., *Ibid.*, p. 370 (1948).
21. Israel, G., Tuck, A., and Soper, F., *Ibid.*, p. 547 (1945).
22. Orazi, O., and Meseri, J., *Anales asoc. quim. argentina*, **37**, 192 (1949); *C. A.*, **44**, 4423 (1950); idem, *Ibid.*, **37**, 263 (1949); *C. A.*, **44**, 5828 (1950); Orazi, O., and Salellas, J., *Anales asoc. quim. argentina*, **38**, 12 (1950); *C. A.*, **44**, 7778 (1950).

A Self-Aligning All-Purpose Glass-Seal Stirring Assembly

In the accompanying figure there is shown a simple device with which a reaction may be stirred while sealed from the atmosphere. Any common glass-rod stirrer is attached to the ball portion of a ball-and-socket joint by means of a short length of rubber pressure tubing. This assembly rests on a socket joint which has been joined to a standard taper joint as illustrated. The ball turns in the socket during stirring and makes an efficient seal. The ball and socket may be lubricated with mineral oil, glycerol, or, in some cases, the solvent used in the reaction. The stirring may be accomplished by any conventional motor. It is desirable, though not necessary, that the stirring rod should fit fairly closely the ball section of the seal. This prevents lateral "play" of the stirring rod.



The mechanism has been found very useful for working under a small pressure of nitrogen, as, for example, in the Grignard reaction. It is smoother and more convenient than the mercury-seal stirrer often used.

Another use is found where reactions must be stirred in a vacuum. The mechanism has been used successfully to stir reactions carried out at 0.2 millimeter pressure. In this case, a heavier lubricant, such as stopcock grease, must be used.

The mechanism has also proved useful in stirring reactions under reflux where the vapors would escape through an unsealed stirring assembly.

In cases where a complete absence of rubber is required, the rubber tubing in the figure may be replaced by a glass ring seal. This, of course, robs the assembly of some of its flexibility of use, in that it may then be used with only one stirrer and one size of flask.

The ball-and-socket variety of glass-seal stirring mechanism has several distinct advantages over another widely used type which consists of a conventional stirring rod revolving in an "exact-bore" glass bearing. It gives a much more efficient and reliable seal and does not need to be carefully aligned as does the latter. In addition, the seal is not so liable to lose its efficiency with wearing as is the "exact-bore" type.

New Eastman Organic Chemicals

P 6741	Benzenephosphonic Acid (Pract.) MP 164°-166°	100 g.	$1.05
	$C_6H_5PO_3H_2$ . . . MW 158.10	500 g.	3.35
P 6750	Benzenephosphonous Acid (Pract.) MP 83°-86°	100 g.	1.05
	$C_6H_5PO_2H_2$ . . . MW 142.10	500 g.	3.35
P 6756	Diethyl *p,p*-azodibenzoate (Pract.) MP 143°-146°	100 g.	2.00
	$C_2H_5OCOC_6H_4N{:}NC_6H_4COOC_2H_5$ . . . MW 326.34	500 g.	8.10
P 6769	Ethylene Carbonate (Pract.) MP 35°-37°	100 g.	1.45
	OCH_2CH_2OCO . . . MW 88.06	500 g.	5.20
6754	2-(*o*-Hydroxyphenyl)benzoxazole MP 124°-126°	10 g.	2.50
	$C_6H_4OC(C_6H_4OH){:}N$ . . . MW 211.21	25 g.	5.50